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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY-DOCKET NO.	CONFIRMATION NO.
09/689,281	10/11/2000	Stephen C. Cosenza	6056-277	1158

23973 7590 04/10/2002

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EXAMINER

BAHAR, MOJDEH

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 04/10/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/689,281

Applicant(s)

CONSENZA ET AL.

Examiner

Mojdeh Bahar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 January 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 8-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response to the first office action of July 5, 2001 submitted January 14, 2002 (Paper No. 11) is acknowledged.

Applicant's remarks and amendments submitted January 14, 2002 in Paper No. 11 are persuasive to remove the rejection under 35 U.S.C. 102 (b) and 112 in the previous office action.

The search for species of active compounds herein has been extended to include the styryl sulfone compound, E-4-fluorostyryl 4-chlorobenzyl sulfone.

Claims 1-7 and 12-22 have been examined insofar as they read on the elected specie and the additional specie discussed immediately above.

This application contains claims 8-11 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-87 and 12-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al. WO 99/18608 and Griggs (Embase Abstract AN 1998287056).

Reddy et al. WO 99/18608 teaches a compound of general formula I and II and III (encompassing both E and Z configurations) employed in a method of treating breast and

prostate tumor cells, and induce apoptosis of such tumor cells while sparing normal cells, see claims 1-9 and abstract.

Reddy et al. WO 99/18608 does not teach a method comprising the administration of compound of general formula I and II and III (encompassing both E and Z configurations) prior to the administration of mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

Griggs (Embase Abstract AN 1998287056) teaches that cytoprotective agents reduce treatment-related toxicity of anticancer therapy. Griggs specifically teaches the employment of cytotoxic agents with paclitaxel, see abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ anticancer paclitaxel along with a cytoprotective agent such as the styryl sulfone compounds of Reddy et al.

One of ordinary skill in the art would have been motivated to employ anticancer paclitaxel along with a cytoprotective agent such as the styryl sulfone compounds of Reddy et al. because both compounds are known to be effective in treating cancer. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be useful for the very same purpose, *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980). Further, the optimization of regimens is within the purview of the skilled artisan.

The elected specie 4-carboxystyryl-4-chlorobenzylsulfone is allowable over prior art. Therefore the methods of both claim 1 and 18, employing the elected specie, 4-carboxystyryl-4-chlorobenzylsulfone is not seen to be taught or fairly suggested by the prior art.

Response to Arguments

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Applicants' arguments regarding the non-obviousness of the instant claims submitted 1/14/02 have been considered but are not found persuasive. Applicant first argues that absent from the combination of the prior art references are the following elements:

(1) the administration of an effective amount of at least one cytoprotective alpha, beta unsaturated aryl sulfone compound, (2) before (3) the administration of a mitotic cell cycle inhibitor or topoisomerase inhibitor.

Note that the administration of the alpha, beta unsaturated styryl sulfone compound, would inherently encompass all the qualities of the compound (i.e., cytoprotection) since a compound and its properties cannot be mutually exclusive. Applicants note that alpha, beta unsaturated aryl sulfone compound differ from the other cytoprotective agents in that they are also operationally cytotoxic to the tumor cell. Note that this very point is taught in Reddy et al., i.e., styryl sulfones induce apoptosis in tumor cells while sparing normal cells. The compounds taught in Reddy are therefore both cytoprotective (as to normal cells) and cytotoxic (as to the tumor cells), see abstract, see also page 8, lines 11-31. Applicant's further argue that amifostine, the cytoprotective agent taught in Griggs does not have the same structure and function as the compounds herein. Note that Griggs was employed to show that cytoprotective agents are known to be used with mitotic cell cycle inhibitors, i.e., paclitaxel.

As to the administration of cytoprotective agent BEFORE the administration of a mitotic cell cycle inhibitor or topoisomerase inhibitor, note that the employment of cytoprotective agents prior to the administration of chemotherapeutic agents is well established in the art, for example mesna is known to be administered prior to ifosfamide. Even if, one were to employ styryl sulfones for their cytotoxic properties, increasing the toxicity of cytotoxic agents employed in

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chemotherapy is also known in the art, i.e., styryl sulfones would be administered prior to paclitaxel.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 on Monday, Tuesday, Thursday and Friday from 8:30 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
April 5, 2002


MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600